AMENDMENTS TO THE CLAIMS

1. A method for the quantification of *in vivo* RNA from a biological sample comprising the steps of:

(a) collecting said biological sample in a tube comprising a compound inhibiting RNA degradation and/or gene induction,

(b) forming a precipitate comprising nucleic acids;

(c) separating said precipitate of step (b) from the supernatant,

(d) dissolving said precipitate of step (c) using a buffer, forming a suspension,

(e) isolating nucleic acids from said suspension of step (d) using an automated device,

(f) dispersing/distributing a reagent mix for RT-PCR using an automated device,

(g) dispersing/distributing the nucleic acids isolated in step (e) within the dispersed reagent mix of step (f) using an automated device, and,

(h) determining the *in vivo* levels of transcripts using the nucleic acid/RT-PCR reagent mix of step (g) in an automated setup.

2. (Currently amended) ~~A~~ The method according to claim 1, whereby steps (a) and (b) are performed simultaneously.

3. (Currently amended) ~~A~~ The method according to claim 1 or 2, whereby said compound of step (a) comprises a quaternary amine surfactant.

4. (Currently amended) ~~A~~ The method according to claim 3, whereby said quaternary amine is tetradecyltrimethyl-ammonium oxalate.

5. (Currently amended) ~~A~~ The method according to claim 1 or 2, whereby said compound of step (a) is a compound inhibiting cellular RNA degradation and/or gene induction as found in a PAXgene™ Blood RNA Tube.

6. (Currently amended) ~~A~~ The method according to ~~any of the claims 1 to 5~~claim 1 or 2, whereby said tube of step (a) is an open or a closed blood collecting tube.

7. (Currently amended) ~~A~~ The method according to ~~any of the claims 1 to 6~~claim 1 or 2, whereby said buffer of step (d) is a guanidine-thiocyanate-containing buffer.

8. (Currently amended) ~~A~~ The method according to claim 7, whereby said guanidine-thiocyanate-containing buffer is a lysis buffer as provided by the MagNa Pure LC mRNA Isolation Kit I (Roche Diagnostics, Molecular Biochemicals).

9. (Currently amended) ~~A~~ The method according to ~~any of the claims 1 to 8~~claim 1or 2, whereby said isolation of nucleic acids of step (e) is performed using RNA-capturing beads.

10. (Currently amended) ~~A~~ The method according to ~~any of the claims 1 to 9~~claim 1 or 2, whereby said automated device of step (e), step (f) and/or step (g) is the MagNA Pure LC Instrument (Roche Diagnostics, Molecular Biochemicals).

11. (Currently amended) ~~A~~ The method according to ~~any of the claims 1 to 10~~claim 1 or 2, whereby said *in vivo* levels are determined using real time PCR.

12. (Currently amended) ~~A~~ The method according to ~~any of the claims 1 to 11~~claim 1 or 2, whereby said quantification is performed using a biological sample of 100 µl.

13. (Original) A method for the quantification of *in vivo* RNA from a biological sample comprising the steps of:

(a) collecting a biological sample in the PAXgene™ RNA tube,

(b) dissociating the surfactant/nucleic acid complex with a guanidine isothiocyanate buffer,

(c) extracting mRNA and/or total RNA using an reproducible automated device,

(d) dispersing/distributing a reagent mix for RT-PCR using an automated device,

(e) dispersing/distributing the nucleic acids isolated in step (c) within the dispersed reagent mix of step (d) using an automated device, and,

(f) quantifying RNA by real time PCR in an automated setup, whereby the RT and the PCR reaction are performed in one step.

14. (Original) A kit for isolating quantifiable *in vivo* RNA from a biological sample comprising:

(a) optionally, a collection tube for biological samples,

(b) a compound inhibiting RNA degradation and/or gene induction,

(c) reagents for automated RNA isolation,

(d) a reagent mix for a simultaneous RT and real-time PCR reaction or separate compounds thereof, allowing the automated dispersion of said mix,

(e) optionally, specific oligonucleotides to perform said RT-PCT reactions, and,

(f) optionally, an instruction manual describing a method for an automated RNA isolation, a method for the automated dispersion of a reagent mix and the dispersion of the isolated nucleic acids for RT- real time PCR, and a method for automated RNA analysis.

15. (Currently amended) ~~A~~ The kit according to claim 14, wherein said compound of part (b)comprises a quaternary amine surfactant ~~is a compound as defined in any of the methods of claims 3 to 5~~.

16. (Currently amended) ~~A~~ The kit according to ~~claims 14 and 15~~claim 14, ~~wherein additionally~~further comprising a buffer ~~is provided as defined in any of the methods of claims 7 to 8~~which is a guanidine-thiocyanate-containing buffer.

17. (Original) A kit for isolating quantifiable *in vivo* RNA from a biological sample comprising:

(a) a PAXgene™ Blood RNA Tube,

(b) a guanidine isothiocyanate buffer,

(c) reagents for automated RNA isolation,

(d) a reagent mix for a simultaneous RT and real-time PCR reaction or separate compounds thereof, allowing the automated dispersion of said mix,

(e) optionally, specific oligonucleotides to perform said RT-PCT reactions, and,

(f) optionally, an instruction manual describing a method for an automated RNA isolation, a method for the automated dispersion of a reagent mix and the dispersion of the isolated nucleic acids for RT- real time PCR, and a method for automated RNA analysis.

18. (Currently amended) A method for the quantification of DNA from a biological sample wherein a method is used as performed for the quantification of RNA according to the ~~methods of any of claims 1 to 13~~ method of claim 1, wherein the RT reaction is skipped and wherein the compound of step (a) also protects the DNA from being degraded.

19. (Currently amended) ~~A~~ The kit for isolating quantifiable DNA from a biological sample according to ~~any of the claims 14 to 17~~claim 14, wherein a reagent mix/compounds for performing said RT reaction is absent.

20. (Currently amended) ~~Use of a method according to any of the claims 1 to 13 or claim 18 or a kit according to any of the claims 14 to 17 or claim 19~~A method for the monitoring/detection of changes of *in vivo* nucleic acids levels in a biological agent present in a biological sample according to claim 1.

21. (Currently amended) ~~Use of a~~The method ~~or a kit~~ according to claim 20 whereby said biological agent is ~~chosen~~ selected from ~~a~~ the group consisting of eukaryotic cells, prokaryotic cells, viruses and phages.

22. (Currently amended) ~~Use of a method according to any of the claims 1 to 13 or claim 18 or a kit according to any of the claims 14 to 17 or claim 19~~A method for the monitoring/detection of changes of *in vivo* nucleic acids of a biological agent in a biological sample, in order to diagnose a certain disease according to claim 1.

23. (Currently amended) ~~Use of a method according to any of the claims 1 to 13 or claim 18 or a kit according to any of the claims 14 to 17 or claim 19~~A method for the monitoring/detection of changes of *in vivo* nucleic acids of a biological agent in a biological sample, in order to screen for a compound for the production of a medicament for curing a disease according to claim 1.

24. (Original) A compound identifiable by a method according to claim 23.

25. (Currently amended) ~~Use of a method or a kit~~The method according to claim 22 ~~and/or~~or 23, wherein said disease is an immuno-related disease.

26. (Currently amended) ~~Use of a method or a kit~~The method according to claim 23, for the detection/monitoring/screening of a compound, wherein said compound is an immunomodulatory compound which may be ~~chosen~~ selected from ~~a~~ the group consisting of eukaryotic cells, prokaryotic cells, viruses, phages, parasites, drugs (natural extracts, organic molecule, peptide, proteins, nucleic acids), medical treatment, vaccine and transplants.

27. (Currently amended) ~~Use of a method according to any of the claims 1 to 13 or claim 18 or a kit according to any of the claims 14 to 17 or claim 19,~~ A method for the detection/monitoring of epitope specific CTLs or immuno-related transcripts according to claim 1.

28. (Currently amended) A method to identify an agent capable of modifying the immunological status of a subject via the analysis of epitope specific CTLs comprising the steps of:

(a) applying an immunomodulatory agent(s) into a subject,

(b) sampling whole blood from said subject,

(c) optionally, pulsing blood cells present in the whole blood sample of step (b) with an identical/similar and/or different immunomodulatory agent as applied in step (a),

(d) collecting pulsed blood cells of step (c) or non-pulsed blood cells of step (b) in a tube comprising a compound inhibiting RNA degradation and/or gene induction, or adding said compound to the pulsed/non-pulsed cells,

(e) forming a precipitate comprising nucleic acids,

(f) separating said precipitate of step (e) from the supernatant,

(g) dissolving said precipitate of step (f) using a buffer, forming a suspension,

(h) isolating nucleic acids from said suspension of step (g) using an automated device,

(i) dispersing/distributing a reagent mix for RT-PCR using an automated device,

(j) dispersing/distributing the nucleic acids isolated in step (h) within the dispersed reagent mix of step (i) using an automated device,

(k) detecting/monitoring/analyzing the *in vivo* levels of epitope specific CTLs-related transcripts in the dispersed solution of step (j) in an automated setup, and,

(l) ~~identify~~ identifying agents able to modify the immunological status of said subject, whereby, in case the agent of step (a) is already present in the subject, step (a) is omitted.

29. (Currently amended) A method to identify an agent capable of modifying the immunological status of a subject:

(a) applying an immunomodulatory agent(s) into a subject,

(b) sampling whole blood from said subject,

(c) optionally, pulsing blood cells present in the whole blood sample of step (b) with an identical/similar and/or different immunomodulatory agent as applied in step(a),

(d) collecting pulsed blood cells of step (c) or non-pulsed blood cells of step (b) in a tube comprising a compound inhibiting RNA degradation and/or gene induction, or adding said compound to the pulsed/non-pulsed cells,

(e) forming a precipitate comprising nucleic acids,

(f) separating said precipitate of step (e) from the supernatant,

(g) dissolving said precipitate of step (f) using a buffer, forming a suspension,

(h) isolating nucleic acids from said suspension of step (g) using an automated device,

(i) dispersing/distributing a reagent mix for RT-PCR using an automated device,

(j) dispersing/distributing the nucleic acids isolated in step (h) within the dispersed reagent mix of step (i) using an automated device,

(k) detecting/monitoring/analyzing the *in vivo* levels of immuno-related transcripts in the dispersed solution of step (j) in an automated setup, and,

(~~m~~l) ~~identify~~ identifying agents able to modify the immunological status of said subject, whereby, in case the agent of step (a) is already present in the subject, step (a) is omitted.

30. (Original) A method for the diagnosis/prognosis/monitoring of a clinical status affecting the immune system in a subject comprising the steps of:

(a) sampling whole blood from said subject in a tube comprising a compound inhibiting RNA degradation and/or gene induction, or adding said compound to the blood cells,

(b) forming a precipitate comprising nucleic acids,

(c) separating said precipitate of step (b) from the supernatant,

(d) dissolving said precipitate of step (c) using a buffer, forming a suspension,

(e) isolating nucleic acids from said suspension of step (d) using an automated device,

(f) dispersing/distributing a reagent mix for RT-PCR using an automated device,

(g) dispersing/distributing the nucleic acids isolated in step (e) within the dispersed reagent mix of step (f) using an automated device,

(h) detecting/monitoring/analyzing the *in vivo* levels of immuno-related transcripts in the dispersed solution of step (g) in an automated setup, and,

(i) detecting/monitoring the change in *in vivo* levels of immuno-related transcripts, and

(j) diagnosing/prognosing/monitoring the disease affecting the immune system.

31. (Original) A method for the diagnosis/prognosis/monitoring of a clinical status affecting the immune system in a subject comprising the steps of:

(a) sampling whole blood from said subject,

(b) pulsing blood cells present in the whole blood sample of step (a) with an identical/similar and/or different immunomodulatory agent as present in the subject,

(c) collecting pulsed blood cells of step (b) in a tube comprising a compound inhibiting RNA degradation and/or gene induction, or adding said compound to the pulsed cells,

(d) forming a precipitate comprising nucleic acids,

(e) separating said precipitate of step (d) from the supernatant,

(f) dissolving said precipitate of step (e) using a buffer, forming a suspension,

(g) isolating nucleic acids from said suspension of step (f) using an automated device,

(h) dispersing/distributing a reagent mix for RT-PCR using an automated device,

(i) dispersing/distributing the nucleic acids isolated in step (g) within the dispersed reagent mix of step (h) using an automated device,

(j) detecting/monitoring/analyzing the *in vivo* levels of immuno-related transcripts in the dispersed solution of step (i) in an automated setup,

(k) detecting/monitoring the change in *in vivo* levels of immuno-related transcripts, and,

(l) diagnosing/prognosing/monitoring the disease affecting the immune system.

32. (Currently amended) ~~Use or a~~The method according to any of claims 25 to 31, wherein the immuno-related disease is ~~chosen~~ selected from the group consisting of autoimmunity, rheumatoid arthritis, multiple sclerosis, cancer (eg. in cancer immunotherapy), immunodeficiencies (eg. in AIDS), allergy, graft rejection ~~or~~ and Graft versus Host Disease (GVHD) (eg. in transplantation), ~~or~~ wherein the immunomodulatory compound or agent influences one of said diseases; or wherein the change of the immuno-related transcripts or the epitope specific CTLs-related or T Helper lymphocyte-related transcripts indicate the presence of one of said diseases; or wherein the immunological status illustrates the status of one of said diseases.

33. (Currently amended) ~~Use or a~~The method according to claim 32, wherein said immuno-related transcript is ~~chosen~~ selected from the group consisting of nucleic acids coding

for chemokine, cytokine, growth factors, cytotoxic markers, transcription factors, members of the TNF-related cytokine-receptor superfamily and their ligands, apoptosis markers, immunoglobulins, T-cell receptor, and any marker related to the activation or the inhibition of the immune system known or to be discovered.

34. (Currently amended) ~~Use or a~~The method according to claim 33, wherein said nucleic acid codes for a marker ~~chosen~~ selected from the group consisting of IL-1ra, IL-1β, IL-2, IL-4, IL-5, IL-9, IL-10, IL-12p35, IL-12p40, IL-13, TNF-α, IFN-γ, IFN-α, TGF-β, and any interleukin or cytokine involved or not in the immune response.

35. (Currently amended) ~~Use or~~The method according to claim 32, wherein said epitope specific CTLs-related or T Helper lymphocyte-related transcript is ~~chosen~~ selected from the group consisting of nucleic acids coding for cytokines, cytokine receptors, cytotoxines, inflammatory or anti-inflammatory mediators, members of the TNF-related cytokine-receptor superfamily and their ligands, G-protein coupled receptors and their ligands, tyrosine kinase receptors and their ligands, transcription factors, and proteins involved in intra-cellular signaling pathways.

36. (Currently amended) ~~Use or a~~The method according to claim 35, wherein said nucleic acid codes for a marker ~~chosen~~ selected from the group consisting of granzyme, perforines, prostaglandins, leukotrienes, immunoglobulin and immunoglobulin superfamily receptors, Fas and Fas ligand, T cell receptor, chemokine and chemokine receptors, protein-tyrosine kinase C, protein-tyrosine kinase A, Signal Transducer and Activator of Transcription (STAT), NF-kB, T-bet, GATA-3, and Oct-2.

37. (New) The kit according to claim 15, whereby said quaternary amine is tetradecyltrimethyl-ammonium oxalate.

38. (New) The kit according to claim 14, whereby said compound of step (b) is a compound inhibiting cellular RNA degradation and/or gene induction as found in a PAXgene™ Blood RNA Tube.

39. (New) The kit according to claim 16, whereby said guanidine-thiocyanate-containing buffer is a lysis buffer as provided by the MagNa Pure LC mRNA Isolation Kit I (Roche Diagnostics, Molecular Biochemicals).